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An Indolent Type of Epstein-Barr Virus-Associated T-Cell-Rich B-Cell Lymphoma of the Skin: Report of a Case

Hitoshi Take, Kazuo Kubota, Toshio Fukuda, Shogo Shinonome, Osamu Ishikawa, and Takuo Shirakura

Department of Medicine, Kusatsu Branch Hospital, Gunma University School of Medicine, Gunma (H.T., K.K., T.S.); Second Department of Pathology, Gunma University School of Medicine, Gunma (T.F.); Third Department of Internal Medicine, Gunma University School of Medicine, Gunma (S.S.); Department of Dermatology, Gunma University School of Medicine, Gunma (O.I.), Japan

A 74-year-old Japanese man presented with systemic lymphadenopathy, hepatosplenomegaly, and erythroderma in December 1991. A characteristic pattern of anti-EBV antibodies was suggestive of latent EBV infection. A skin tumor biopsied in April 1993 contained biclonal EBV genomes diffusely in the infiltrate of polyclonal T cells and monoclonal B cells. The clinical course was rather mild in contrast to that of classical EBV-associated disorders. Our case was considered a rare indolent type of EBV-associated T-cell-rich B-cell lymphoma of the skin. © 1996 Wiley-Liss, Inc.

Key words: Epstein-Barr virus, indolent type, skin involvement, T-cell-rich B-cell lymphoma

INTRODUCTION

Epstein-Barr virus (EBV) has been associated with a growing number of monoclonal and polyclonal B- and T-lymphoproliferative diseases [1–3]. These disorders usually arise in more or less immunosuppressed patients and show aggressive clinical behavior [1,3–5]. In the following report, we describe an additional but unusual case of EBV-associated cutaneous B-cell lymphoma, which has clinically as well as pathologically unique characteristics.

CASE REPORT

A 74-year-old Japanese man presented with lymphadenopathy, hepatosplenomegaly, and generalized erythroderma in December 1991. The antibody pattern against EBV was suggestive of chronic EBV infection, showing elevated titers of IgG to viral capsid antigen (VCA) and early antigen (EA) (5,120 and 1,280, respectively), while lacking a reaction to Epstein-Barr nuclear antigen (EBNA) at 10 [1,6]. Other laboratory data were normal except for mild to moderately elevated levels of hepatobiliary enzymes. Biopsies from cervical and inguinal lymph nodes revealed no obvious infiltration of atypical cells. A skin specimen from the back showed a dermal infiltrate of homogeneous small lymphoid cells, presenting diffuse staining of T-lineage marker CD45RO and only limited staining of B-lineage marker CD20. A week of treatment with 500 mg/day of intravenous acyclovir was given in February 1992 but failed to alter either the antibody pattern or the clinical features. In April 1993, a skin tumor of 2–3 cm in diameter was found on his neck. Computed tomography (CT) scan of the whole body revealed hepatosplenomegaly, while lymphadenopathy and extranodal lesions were absent. Antibody titers to VCA, EA, and EBNA were 5,120, 2,560, and 10, respectively. A series of detailed examination was compatible with the characteristics of T-cell-rich B-cell lymphoma, as detailed below. The patient received a total of two courses of combined chemotherapy consisting of vincristine, cyclophosphamide, prednisolone, and Adriamycin (VEPA therapy) since May 1993, to which the tumor showed a good response. No remarkable change was observed in clinical status and the pattern of anti-EBV antibodies. The patient died of pneumonia in June 1994.

Histologic studies of the skin tumor demonstrated an effacement of dermal architecture by a marked infiltrate

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Address reprint requests to Dr. Hitoshi Take, Department of Medicine, Kusatsu Branch Hospital, Gunma University School of Medicine, Kusatsu, Gunma 377-17, Japan.

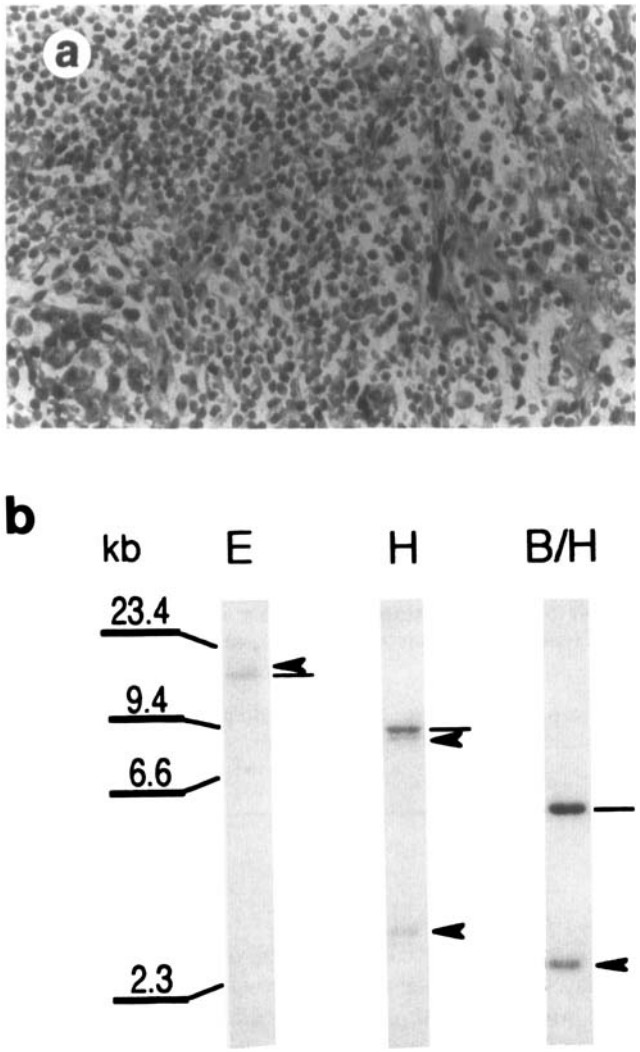

Fig. 1. a: In situ hybridization using EBER-specific oligonucleotide probe. Diffuse presence of EBV DNA in the infiltrate is evident. ×300. b: Southern blot analysis of the gene rearrangements in the infiltrate after digestion by restriction endonuclease *Eco*RI (E), *Hin*dIII (H), and *Bam*HI–*Hin*dIII (B/H), using the JH probe. Arrowheads, rearranged bands; *bars*, germline bands.

of lymphoid cells. The infiltrate was mainly composed of CD45RO-positive cells with small to intermediate nuclei. The CD20-positive cells were scarce and morphologically variable, from small lymphoid cells to large dysplastic cells. Interestingly, those large cells were only stained with CD20. Southern analysis for the presence of EBV in the tumor demonstrated two hybridization bands, indicating biclonal proliferation of EBV (data not shown). Using the probe of EBV-encoded transcripts, EBER, which has been designed for the detection of latent EBV infection [7], the EBV-specific signal was diffusely identified in the infiltrate (Fig. 1a). A monoclonal population of B-lineage cells was also demonstrated by Southern analysis (Fig. 1b). On the other hand, clonotypic analysis of T-cell receptor Vβ genes showed a polyclonal pattern (data not shown).

DISCUSSION

T-cell-rich B-cell lymphoma, a lately recognized B-cell lymphoma variant characterized by a minor population of neoplastic B cells existing in a background of predominant polyclonal T cells [8,9]. Neoplastic B cells occasionally contain monoclonal EBV genomes, in which an early association between the virus and the transformed cells has been suggested [10]. It is also likely in this case that the neoplastic B cells were the primary source of EBV, which may have expanded monoclonally into the accumulated reactive T cells [8,10]. The biclonal EBV possibly represented an original clone and its derivative clone; thus, the neoplastic B cells carrying the derivative EBV clone may have gained an inherent growth advantage and led to biclonal expansion at the tumor site. Also, the clinical course of this case is of interest, presenting no apparent disease progression except for the development of the VEPA-sensitive small skin tumor. This finding is in clear contrast to that of previously reported cases of EBV-associated lymphoproliferative disorders that commonly exhibit aggressive clinical behavior [1,3]. However, it remains uncertain whether the unique indolence was attributable to the phenotype of expanding EBV or the type of lymphocytes infected by EBV and whether this case represents a novel clinical entity. Additional cases are necessary to address these issues.

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